

Table 1: Primers for SNP genotyping of CD81 SNPs with FP-TDI method

| gene/rs | allele | PCR primer name | PCR Primer 1, 2 | SNP primer name | SNP Primer 3, 4 |
|-----------|--------|-----------------|--------------------------|-----------------|-----------------------------|
| rs600146 | R | 01657 | GAGCGGGATTTGTAACCTCTG | | |
| | A/G | 01658 | AGGAAGATCTACCCCTCACTTG | 01690 | TGACTGTGGACATCGGAACTC |
| rs521240 | R | 01661 | CACTGTTCTACTGGCTTG | 01693 | TGGCTGTGGATGGGG |
| | A/G | 01662 | CATTCCAAGTGTAGCACTCCT | | |
| rs800158 | R | 01665 | TGTGTAACCTGTATGGAAAAA | | |
| | A/G | 01666 | CTGAGTGTGCTGTCCACTTA | 01698 | AGCCAGTGTCCAATCGTCC |
| rs800163 | Y | 01669 | GATGAAAGGGATATCCAGAGAG | 01701 | TGGCTGAATAAGGAAGATCTGTC |
| | C/T | 01670 | ACCAGGAGTTCTGATGTCTAAG | | |
| rs800136 | Y | 01244 | CTGATCATAGGGGAAGAACTATC | 01276 | TCCCTTCTATTCTAGTGAGTTCACTG |
| | C/T | 01245 | AAAAAGCAACCAAGGTAAATAAAT | | |
| rs800137 | Y | 01246 | AGAAAGGTCTCTGTCAAACAT | 01278 | CCAAAATGCTGGGAGATGGCA |
| | C/T | 01247 | TCTTCTCCCTCCCTGTGTGA | | |
| rs164688 | S | 01252 | ATTGTGTATTTCGTATTCACTG | | |
| | C/G | 01253 | AGTTTATGTGCCAAGGTTAAG | 01285 | GTACAGTAAATCAGGACAACCTGAAAG |
| rs651842 | R | 01256 | GAGGTGACAAATGGATACTCTG | | |
| | A/G | 01257 | AGACAGCAAGAGTGTGAGTGT | 01288 | TGTTGAAGGTGGAGTGTG |
| rs800334 | K | 01264 | CTAAACCAAAAGTGTGAAAATTGA | | |
| | G/T | 01265 | AGACCCCTGTCTCAAATAAAAT | 01296 | ACCTCTCTCACACACCCGA |
| rs2522012 | K | 01268 | TGGCTAGAGTTGATGTGTG | 01299 | CGCTGGGGCGGCTCT |
| | G/T | 01269 | GAGAGGCTAGGATTGTATGTAC | | |
| rs2522013 | M | 01270 | TGGCTAGAGTTGATGTGTG | | |
| | A/C | 01271 | GAGAGGGTAGGAATTGTATAC | 01301 | CTGGGGAAAGGGCGC |
| rs800335 | Y | 01272 | TGGCTAGAGTTGATGTGTG | | |
| | C/T | 01273 | GAGAGGGTAGGATTGTATGTAC | 01303 | GGGACTTGGGAGGAAGGAC |
| rs800343 | R | 01679 | CTGGTTGTTGGATGTGTAAA | | |
| | A/G | 01680 | GAAGAATGTCTTGACTGTG | 01712 | GGGTTTAATCACAGGCATTAGTGCTG |
| rs800344 | R | 01681 | CTGGTTGTTGGATGTGTAAA | | |
| | A/G | 01682 | GAAGAATGTCTTGACTGTG | 01714 | TGAAAGGTGGCGGAATTACT |
| rs753136 | Y | 01685 | CAAAGTGAACGTGAAAGAAC | 01717 | CCAGCCCTACAGGTGCAC |
| | C/T | 01686 | TTCACTCCCTCACAGAAGAC | | |

Fig. 1

rs800136

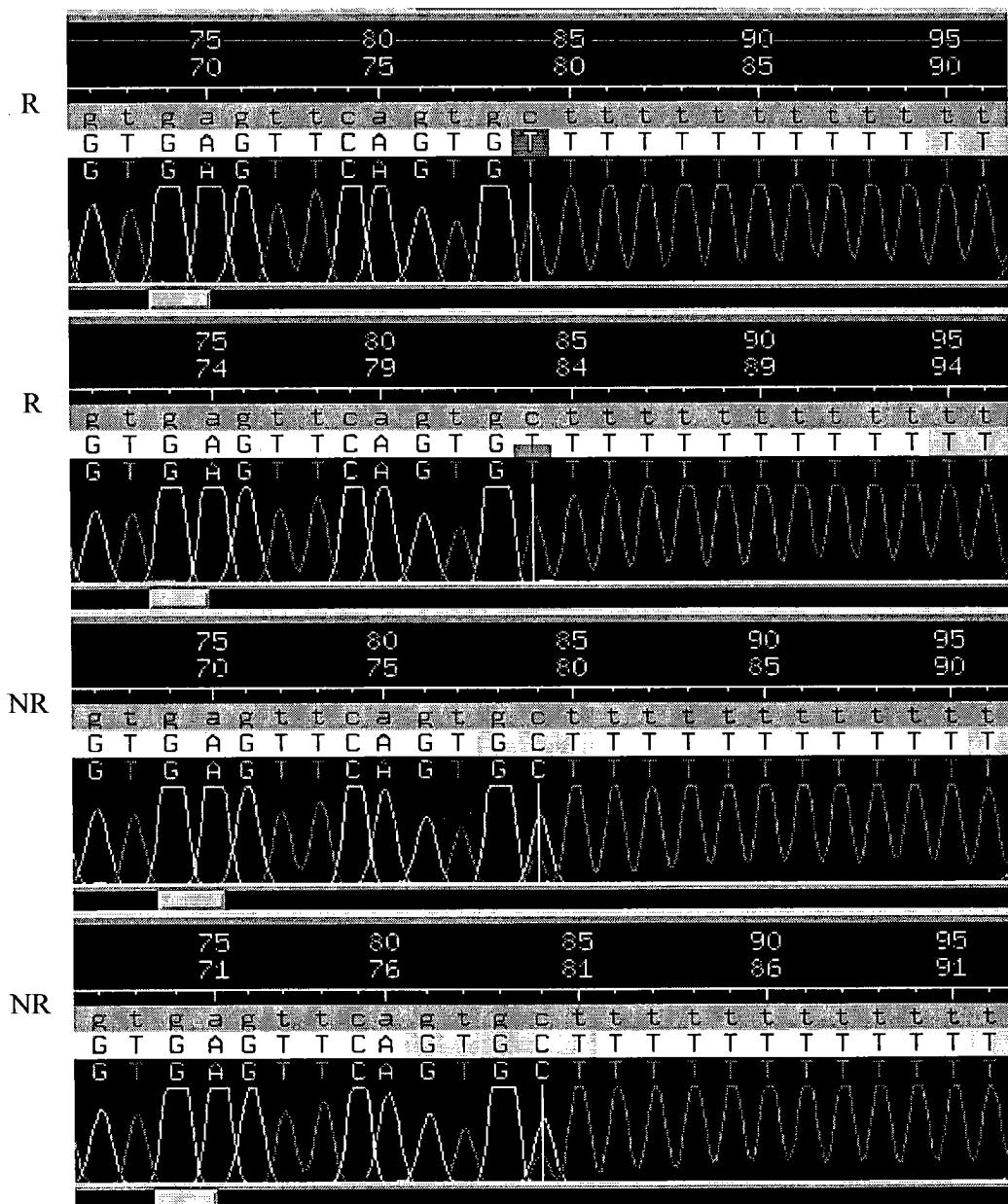


Fig. 2

rs800137

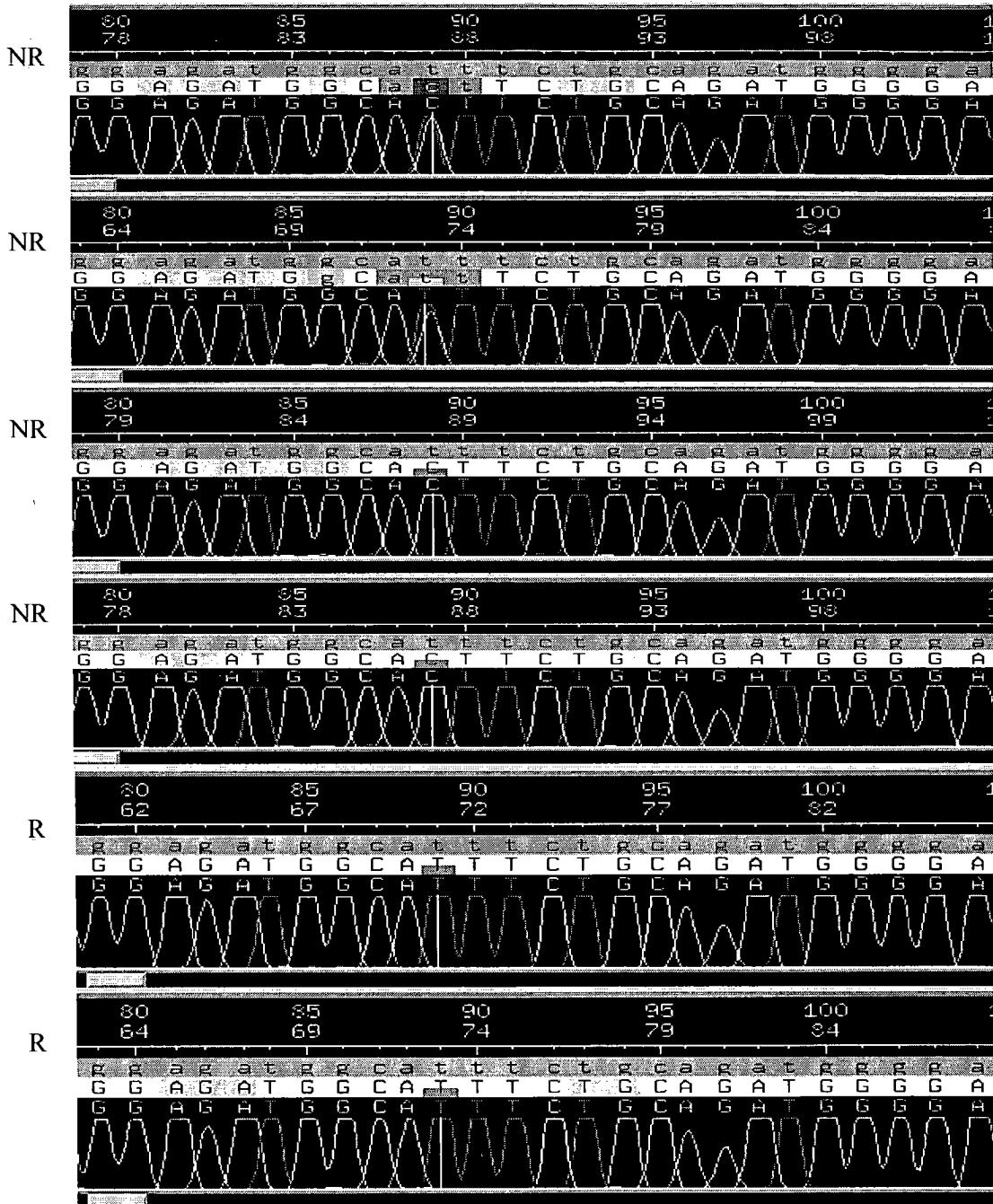


Fig. 3

rs800334

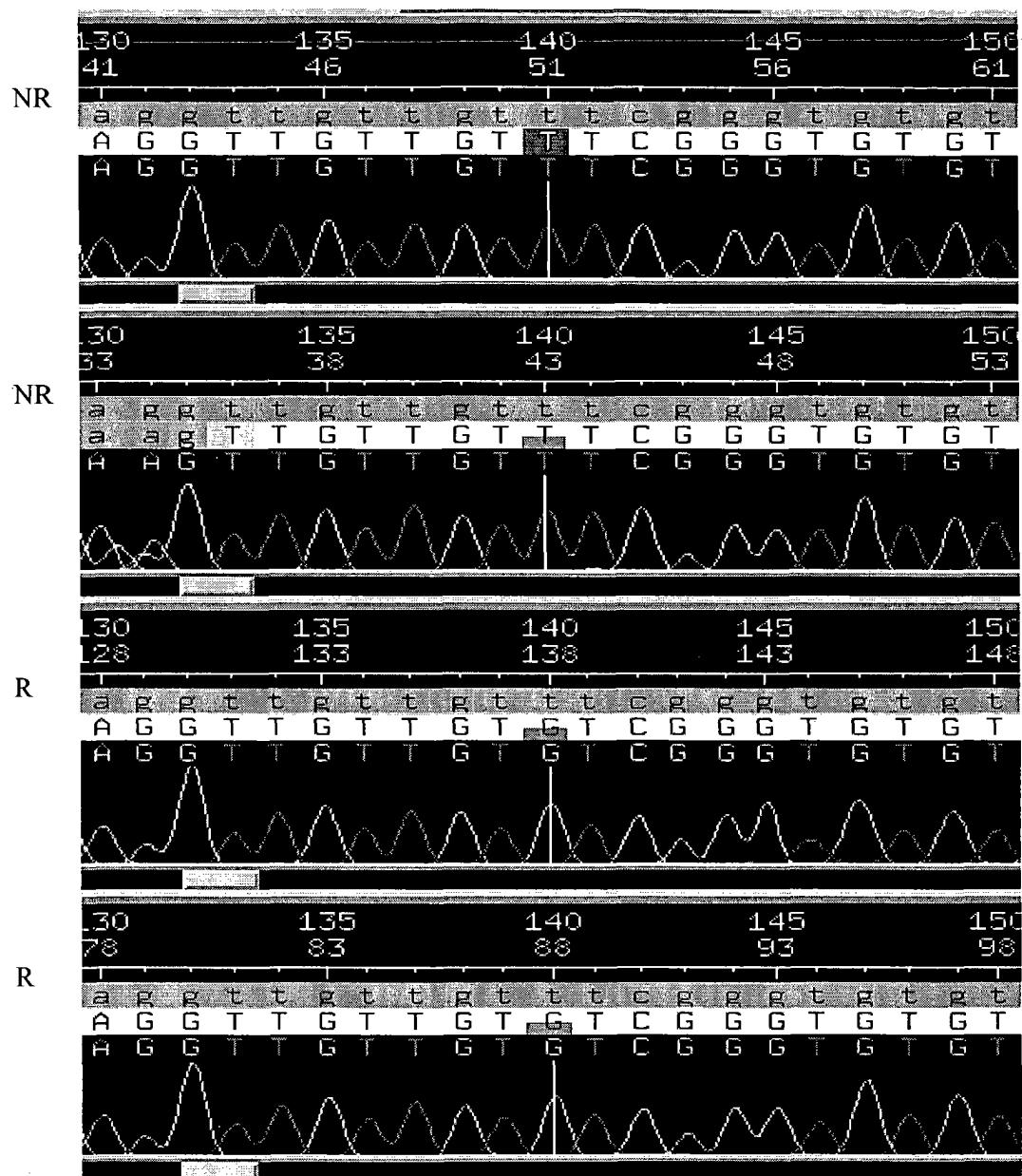


Fig. 4

Chromosome position 1989603

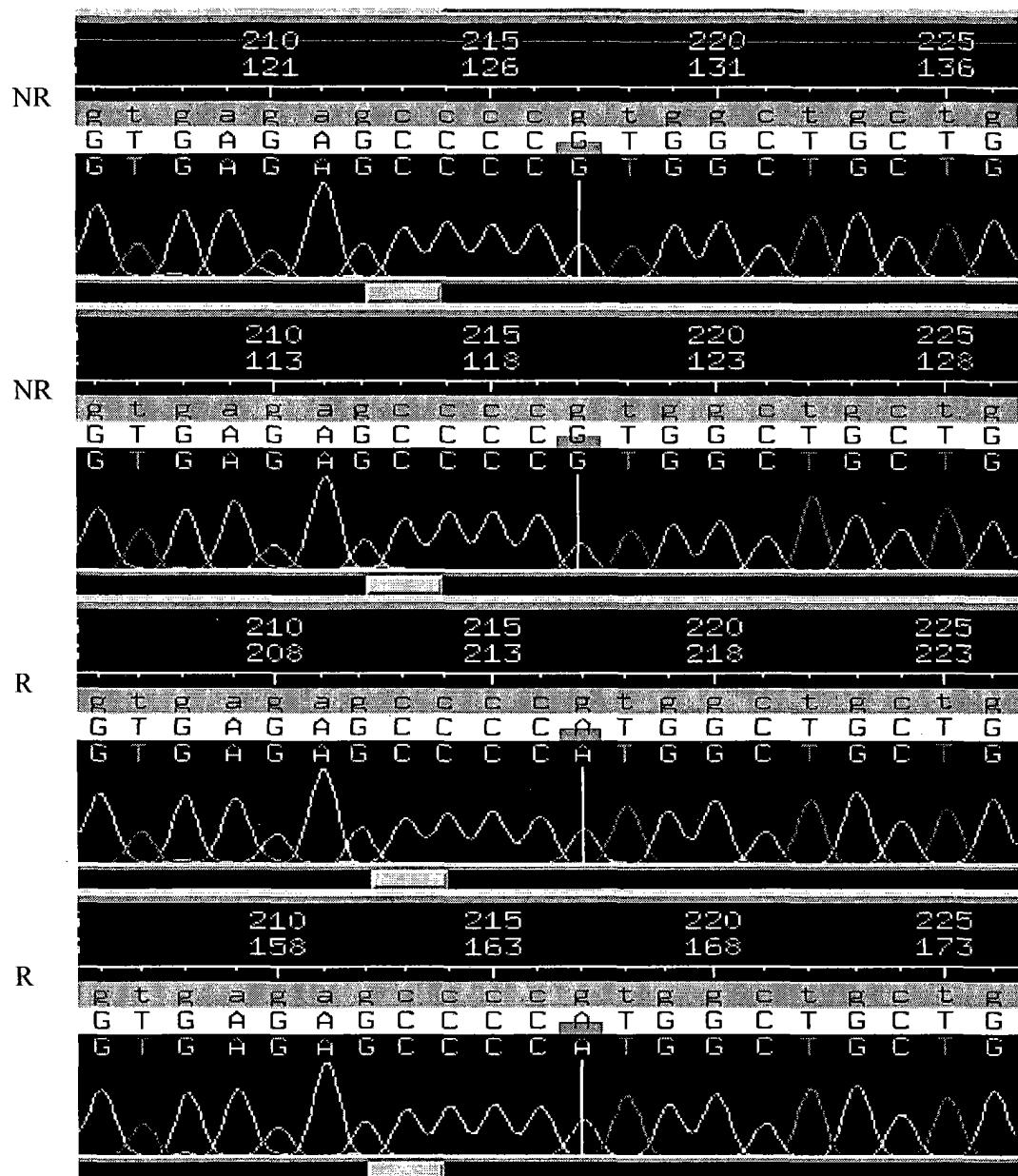


Fig. 5

rs2522012, rs2522013

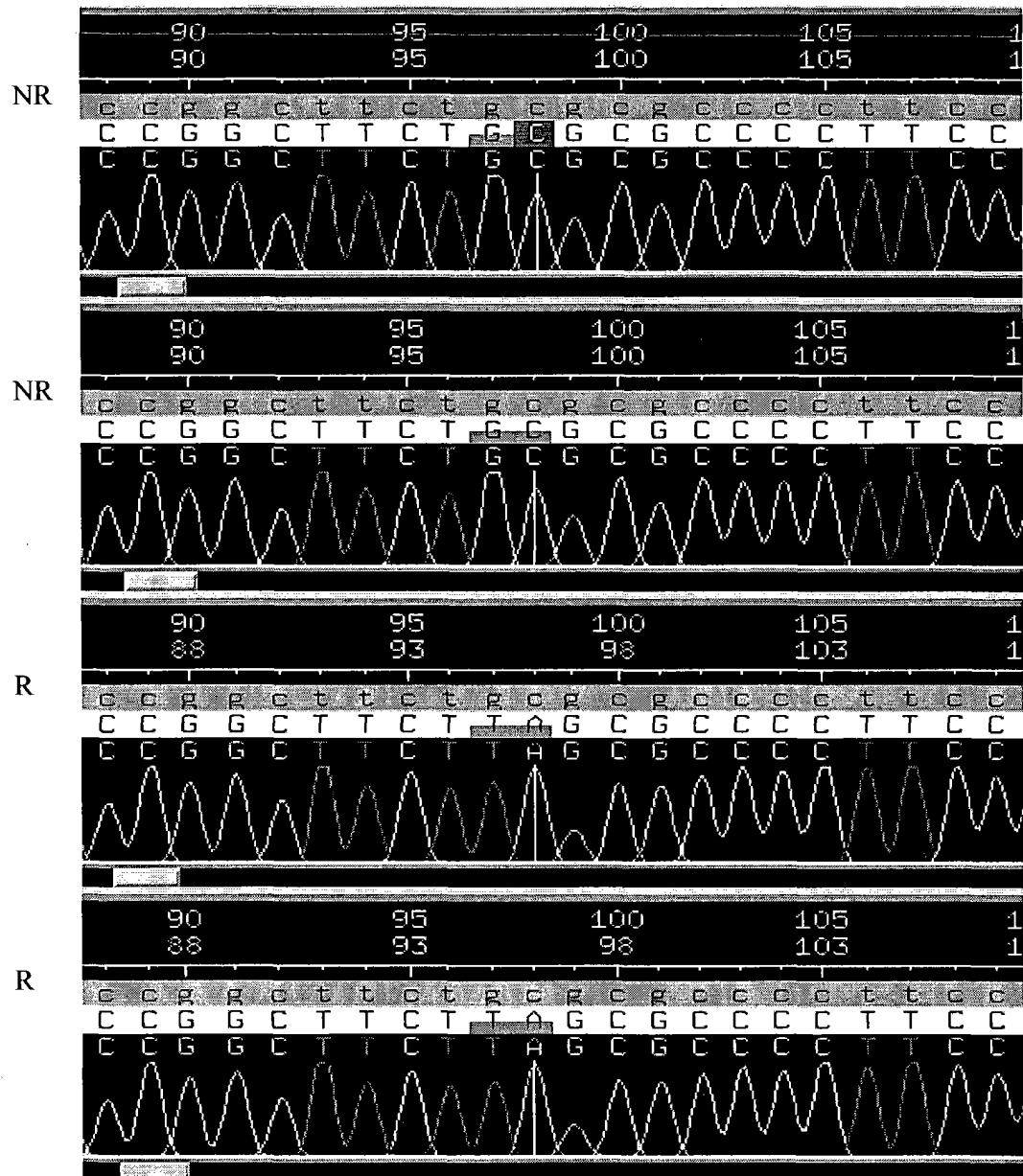


Fig. 6

rs800335

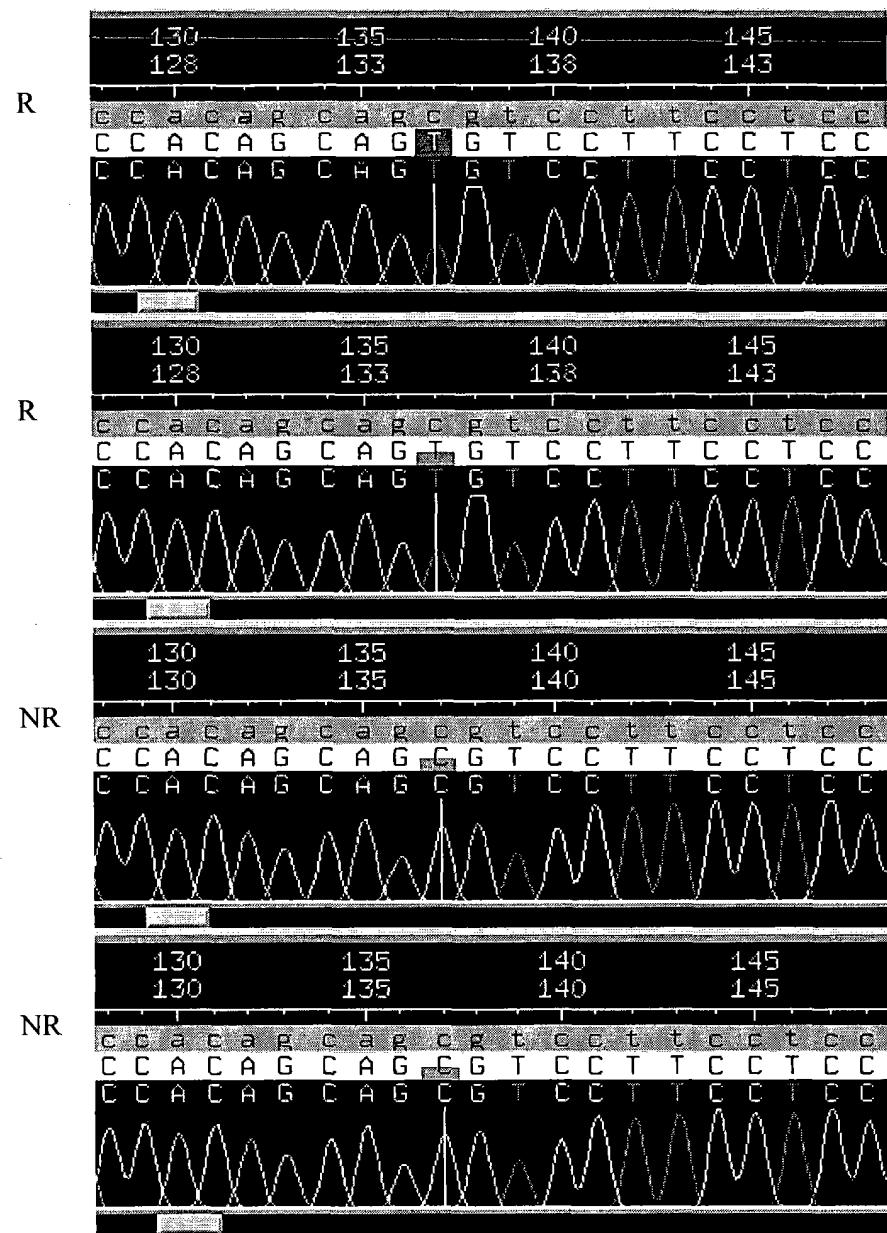


Fig. 7

Table 2: Distribution of CD81 SNPs in Chinese HCV infected patients

| SNP | Location in CD81 genome | rs # | Nucleotide substitution | Allelic frequency | Genotype frequency |
|-----|-------------------------|-----------|-------------------------|-------------------|------------------------------|
| 1 | 1949368 | rs800146 | G/A | G=64.3%, A=35.7% | GG=40.7%, GA=47.3%, AA=12.0% |
| 2 | 1953512 | rs2321240 | G/A | G=74.0%, A=26.0% | GG=55.4%, GA=37.0%, AA=7.6% |
| 3 | 1958563 | rs800158 | G/A | G=38.0%, A=62.0% | GG=15.2%, GA=45.7%, AA=39.1% |
| 4 | 1963385 | rs800163 | C/T | C=39.1%, T=60.9% | CC=16.3%, CT=45.7%, TT=38.0% |
| 5 | 1975622 | rs800136 | C/T | C=54.3%, T=45.7% | CC=29.3%, CT=50.0%, TT=20.7% |
| 6 | 1976158 | rs800137 | C/T | C=54.3%, T=45.7% | CC=29.3%, CT=50.0%, TT=20.7% |
| 7 | 1978278 | rs1164688 | G/C | G=65.8%, C=34.2% | GG=43.5%, GC=44.5%, CC=12.0% |
| 8 | 1982077 | rs2651842 | G/A | G=47.8%, A=52.2% | GG=22.8%, GA=50%, AA=27.2% |
| 9 | 1989526 | rs800334 | G/T | G=47.7%, T=52.3% | GG=23.3%, GT=48.8%, TT=27.9% |
| 10 | 1989603 | | G/A | G=54.1%, A=45.9% | GG=29.1%, GA=50.0%, AA=20.9% |
| 11 | 1991149 | | G/A | G=98.9%, A=1.1% | GG=98.9%, GA=0.0%, AA=1.1% |
| 12 | 1991241 | | C/T | C=0.5%, T=99.5% | CC=0%, CT=1.1%, TT=98.9% |
| 13 | 1991254 | rs2322012 | G/T | G=54.9%, A=45.1% | GG=30.4%, GA=48.9%, AA=20.7% |
| 14 | 1991255 | rs2322013 | C/A | C=54.9%, A=45.1% | CC=30.4%, CA=48.9%, AA=20.7% |
| 15 | 1991294 | rs80035 | C/T | C=54.9%, T=45.1% | CC=30.4%, CT=48.9%, TT=20.7% |
| 16 | 1913110 | | I/N | I=2.2%, N=97.8% | II=1.1%, IN=2.2%, NN=96.7% |
| 17 | 2009970 | rs800343 | G/A | G=60.4%, A=39.6% | GG=60.4%, GA=0.0%, AA=39.6% |
| 18 | 2010006 | rs800344 | G/A | G=58.8%, A=41.2% | GG=36.3%, GA=45.0%, AA=18.7% |
| 19 | 2020475 | rs753136 | C/T | C=67.9%, T=32.1% | CC=44.6%, CT=46.7%, TT=8.7% |

Fig. 8

Table 3: Association of CD81 SNPs with treatment response of HCV patients to interferon- α and ribavirin combined therapy

| SNP | Location in CD81 genome | rs # | Nucleotide substitution | Genotype P-value | Allelic P-value | Genotype Odds ratio | Allelic Odds ratio |
|-----|-------------------------|------------|-------------------------|------------------|-----------------|---------------------|--------------------|
| 1 | 1949368 | rs800146 | G/A | 0.3852 | | | 1.32(0.72-2.45) |
| 2 | 1953512 | rs2521240 | G/A | 0.9473 | | | 1.14(0.59-2.22) |
| 3 | 1958563 | rs800158 | G/A | 0.6607 | | | 0.76(0.42-1.40) |
| 4 | 1963385 | rs800163 | C/T | 0.521 | | | 1.29(0.71-2.36) |
| 5 | 1975622 | rs800136 | C/T | 0.1079 | 0.0435 | 0.52(0.21-1.31) | 0.54(0.30-0.98) |
| 6 | 1976158 | rs800137 | C/T | 0.1079 | 0.0435 | 0.52(0.21-1.31) | 0.54(0.30-0.98) |
| 7 | 1978278 | rs1164688 | G/C | 0.3676 | | | 1.23(0.66-1.27) |
| 8 | 1982077 | rs2651842 | G/A | 0.1290 | | | 0.55(0.31-1.00) |
| 9 | 1989526 | rs800334 | G/T | 0.0454 | 0.0119 | 3.29(1.07-10.12) | 2.2(1.19-4.07) |
| 10 | 1989603 | pos1989603 | G/A | 0.0341 | 0.0101 | 3.61(1.08-12.09) | 2.25(1.21-4.18) |
| 11 | 1991149 | pos1991149 | G/A | 1.0 | | | |
| 12 | 1991241 | pos1991241 | C/T | 0.4615 | | | |
| 13 | 1991254 | rs2522012 | G/T | 0.0331 | 0.0131 | 0.24(0.07-0.79) | 0.47(0.26-0.86) |
| 14 | 1991255 | rs2522013 | C/A | 0.0331 | 0.0131 | 4.19(1.27-13.86) | 2.12(1.17-3.85) |
| 15 | 1991294 | rs800335 | C/T | 0.0331 | 0.0131 | 0.24(0.07-0.79) | 0.47(0.26-0.86) |
| 16 | 191310 | pos191310 | I/N | 0.2103 | | | 0.85(0.12-6.20) |
| 17 | 2009970 | rs800343 | G/A | 0.8013 | | | 0.87(0.48-1.56) |
| 18 | 2010006 | rs800344 | G/A | 0.9983 | | | 1.00(0.55-1.81) |
| 19 | 2020475 | rs753136 | C/T | 0.2933 | | | 1.62(0) |

Fig. 9

Table 4: CD81-SNPrs800136 alleles and associated treatment response status

| | responder | Non-responder |
|---------------------------|-----------|---------------|
| CD81-SNPrs800136 C allele | 46 | 56 |
| CD81-SNPrs800136 T allele | 52 | 32 |

$\chi^2 = 4.0764$, P value = 0.0435, OR = 0.54, 95% CI = (0.30, 0.98)

Fig. 10

Table 5: CD81-SNPrs800137 alleles and associated treatment response status

| | responder | Non-responder |
|---------------------------|-----------|---------------|
| CD81-SNPrs800137 C allele | 46 | 56 |
| CD81-SNPrs800137 T allele | 52 | 32 |

$\chi^2 = 4.0764$, P value = 0.0435, OR = 0.54, 95% CI = (0.30, 0.98)

Fig. 11

Table 6: CD81-SNPsrs800334 alleles and associated treatment response status

| | responder | Non-responder |
|----------------------------|-----------|---------------|
| CD81-SNPsrs800334 G allele | 52 | 29 |
| CD81-SNPsrs800334 T allele | 40 | 49 |

$\chi^2 = 6.3310$, P value = 0.0119, OR = 2.2, 95% CI = (1.19, 4.07)

Table 7: CD81-SNPsrs800334 genotypes and associated treatment response status

| | responder | Non-responder |
|----------------------------------|-----------|---------------|
| CD81-SNPsrs800334 GG genotype | 15 | 31 |
| CD81-SNPsrs800334 GT+TT genotype | 5 | 34 |

$\chi^2 = 3.29$, P value = 0.0321, OR = 3.29, 95% CI = (1.07, 10.12)

Fig. 12

Table 8: CD81-SNP pos1989603 alleles and associated treatment response status

| | responder | Non-responder |
|------------------------------|-----------|---------------|
| CD81-SNP pos1989603 A allele | 52 | 27 |
| CD81-SNP pos1989603 G allele | 42 | 49 |

$\chi^2 = 6.6182$, P value = 0.0101, OR = 2.25, 95% CI = (1.21, 4.18)

Table 9: CD81-SNP pos1989603 genotypes and associated treatment response status

| | responder | Non-responder |
|------------------------------------|-----------|---------------|
| CD81-SNP pos1989603 AA genotype | 14 | 31 |
| CD81-SNP pos1989603 AG+GG genotype | 4 | 34 |

$\chi^2 = 5.1402$, P value = 0.0234, OR = 3.61, 95% CI = (1.08, 12.09)

Fig. 13

Table 10: CD81-SNPrs2522012 alleles and associated treatment response status

| | responder | Non-responder |
|----------------------------|-----------|---------------|
| CD81-SNPrs2522012 G allele | 45 | 54 |
| CD81-SNPrs2522012 T allele | 53 | 30 |

$\chi^2 = 6.1512$, P value = 0.0131, OR = 0.47, 95% CI = (0.26, 0.86)

Table 11: CD81-SNPrs2522012 genotypes and associated treatment response status

| | Responder | Non-responder |
|---------------------------------|-----------|---------------|
| CD81-SNPrs800334 GG+GT genotype | 34 | 38 |
| CD81-SNPrs800334 TT genotype | 15 | 4 |

$\chi^2 = 6.0882$, P value = 0.0136, OR = 0.24, 95% CI = (0.07, 0.79)

Fig. 14

Table 12: CD81-SNPrs2522013 alleles and associated treatment response status

| | responder | Non-responder |
|----------------------------|-----------|---------------|
| CD81-SNPrs2522012 A allele | 53 | 30 |
| CD81-SNPrs2522012 C allele | 45 | 54 |

$\chi^2 = 6.1512$, P value = 0.0131, OR = 2.12, 95% CI = (1.17, 3.85)

Table 13: CD81-SNPrs2522013 genotypes and associated treatment response status

| | Responder | Non-responder |
|---------------------------------|-----------|---------------|
| CD81-SNPrs800334 AA genotype | 15 | 4 |
| CD81-SNPrs800334 AC+CC genotype | 34 | 38 |

$\chi^2 = 6.0882$, P value = 0.0136, OR = 0.24, 95% CI = (0.07, 0.79)

Fig. 15

Table 14: CD81-SNPrs800335 alleles and associated treatment response status

| | responder | Non-responder |
|----------------------------|-----------|---------------|
| CD81-SNPrs2522012 C allele | 45 | 53 |
| CD81-SNPrs2522012 T allele | 53 | 30 |

$\chi^2 = 6.1512$, P value = 0.0131, OR = 0.47, 95% CI = (0.26, 0.86)

Table 15: CD81-SNPrs800335 genotypes and associated treatment response status

| | Responder | Non-responder |
|---------------------------------|-----------|---------------|
| CD81-SNPrs800334 CC+CT genotype | 34 | 38 |
| CD81-SNPrs800334 TT genotype | 15 | 4 |

$\chi^2 = 6.0882$, P value = 0.0136, OR = 0.24, 95% CI = (0.07, 0.79)

Fig. 16

Haplotype Block Information

CD81

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|

HAP Map: 16 SNPs in 9 HAP Blocks

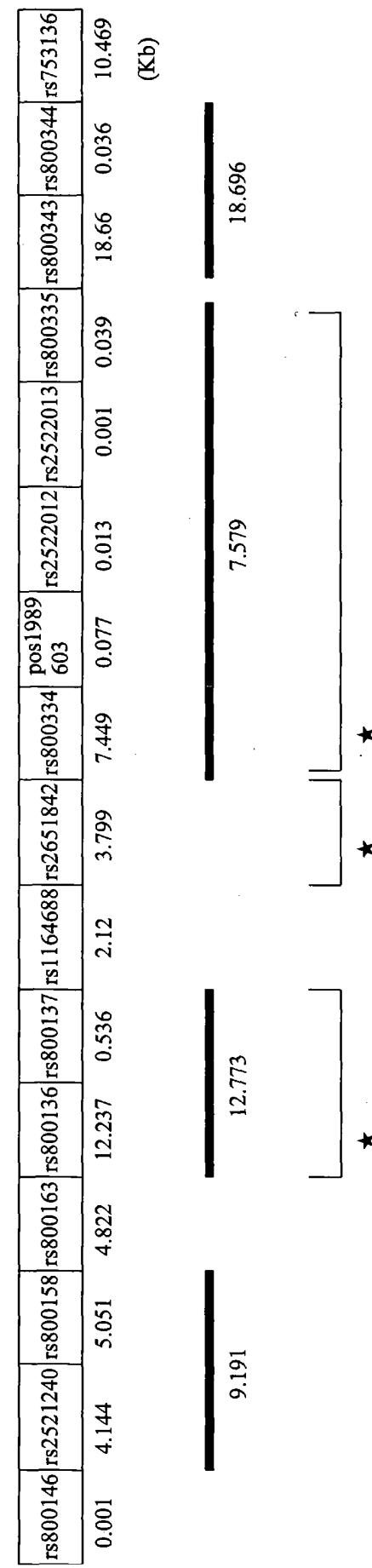


Fig. 17

Table 16: CD81-SNPs rs800136 and rs800137 haplotype and associated treatment response status

| | Responder | Non-responder |
|--------------|-----------|---------------|
| CC haplotype | 46 | 52 |

$\chi^2 = 4.0746$, P value = 0.0435, OR = 1.8370

Fig. 18

Table 17: CD81-SNPs rs800334, pos1989603, rs2522012, rs2522013, rs800335 haplotypes and associated treatment response status

| | Responder | Non-responder |
|-----------------|-----------|---------------|
| TGGCC haplotype | 51 | 43 |
| GATAT haplotype | 30 | 52 |

$\chi^2 = 5.1343$, P value = 0.0235, OR = 1.9767 for TGGCC haplotype
 $\chi^2 = 5.4980$, P value = 0.0190, OR = 0.4915 for GATAT haplotype

Fig. 19